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Newcastle Disease Vaccines: From Conventional Limitations to Chitosan Nanovaccine Solutions

Fakhar Abbas[1*], Ahmad Raza[1], Muhammad Awais Nadeem[1], Muhammad Qasim[2] and Muhammad Usman[3]

1. Faculty of Veterinary Sciences, University of Agriculture Faisalabad, Pakistan
2. Institute of Microbiology, Government College University Faisalabad, Pakistan
3. Department of Microbiology, University of veterinary and animal sciences, Jhang, Pakistan

*Corresponding Author: **fakharabbas4596@gmail.com**

ABSTRACT

Newcastle Disease (ND) is considered one of the most important infectious diseases that cause economic loss in the worldwide chicken industry. Given the genotypic variations of the Newcastle disease virus (NDV) and the obstacles in maintaining cross-immunity, this article explores the current limits of conventional ND vaccines, emphasizing the practical applications of chitosan, a biodegradable biomaterial, in the production of next-generation nanovaccine delivery platforms. Relative to conventional vaccines, chitosan-based nanoparticles present both types of immunity (cellular, humoral), sustained antigen delivery, and optimized mucosal immune responses. The advantages of chitosan nanovaccine in chicken rearing systems are shown in this research, including lower vaccine cost, enhanced disease control, and strengthened biosecurity. The article finishes by explaining what can happen in the future regarding the use of nanoparticles for nanovaccines, legal requirements, and the areas where the research is still needed in the poultry sector.

Keywords: Newcastle Disease Virus, Conventional Vaccines, Chitosan, Nanovaccines, Poultry Production

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Introduction

A highly contagious viral disease that affects chicken species globally, Newcastle disease (ND) causes substantial financial losses in both commercial and backyard agricultural enterprises [1]. Newcastle disease virus (NDV), an enveloped, negative-sense, single-stranded RNA virus that is a member of the *Paramyxoviridae* family, is the causal agent. Respiratory symptoms, neurological indications, reproductive failure, and, in severe cases (virulent systemic ND), multi-organ involvement with significant mortality rates are just a few of the disease's many clinical manifestations [2]. More than twenty distinct genotypes of NDV strains have been identified worldwide as a result of their ongoing evolution and genetic diversification, which has complicated vaccination plans and disease control initiatives [3].

For over six decades, vaccination has been the primary tool for ND control in poultry production systems. However, conventional vaccines face significant challenges in maintaining protective immunity against the genetically diverse NDV strains currently circulating in endemic regions [4].

Limitations of Conventional Newcastle Disease Vaccines:

The incapacity of traditional Newcastle disease vaccines to offer cross-protection against genetically distinct NDV isolates is their main drawback. Genotype II strains (La Sota and other lentogenic strains) constitute the basis for the most popular commercial ND vaccines, which were created decades ago when these strains were common. However, La Sota and currently circulating genotype VII strains have only 87–89% amino acid sequence homologies, according to genetic research, indicating substantial antigenic diversity [5]. In regions where virulent genotype VII NDV strains are endemic, the use of genotype II-based vaccines frequently results in breakthrough infections characterized by respiratory disease, neurological signs, and reproductive failures in vaccinated poultry. Studies have documented vaccination failures in commercial broiler and layer farms using standard ND vaccines, leading to significant economic losses and necessitating multiple re-vaccination protocols that are economically inefficient [6].

Chitosan: A Promising Nanomaterial for Vaccine Delivery:

Chitosan is a naturally occurring polysaccharide that is produced by deacetylating chitin, which is the main constituent of the exoskeletons of arthropods, including insects and crustaceans. Repeating units of β-(1→4)-2-amino-2-deoxy-D-glucopyranose (N-acetyl glucosamine) connected by glycosidic linkages make up the biopolymer. Chitosan's distinct chemical structure gives it a variety of useful characteristics that make it perfect for vaccine delivery applications [7]. Chitosan has the ability to stick to the mucous membranes, trigger immune responses, and be decomposed by the lysozyme and other enzymes present in the host organism. Chitosan contains a positive electrical charge, which aligns with the normal body condition (normal pH), whereas other biopolymers used in drug shipment are neutral or negatively charged. Chitosan is one of the natural biopolymers that is positively charged under biological conditions. The mucosal epithelial cells and the antigens are generally negatively charged since the chitosan is positively charged, so it is easily pulled towards them, just like a magnetic material. That's why chitosan is approved to be excellent in binding with the mucosal surfaces and antigens. This electrostatic attraction explains the mechanism by which chitosan improves the mucosal immunity and sustains antigen release. Because of these abilities, some health authorities in different countries can be called GRAS (Generally Recognized as Safe). Due to its safe nature for living tissues, companies do not require laboratory testing for the production of human and animal vaccines [8].

Chitosan nanoparticles are prepared by using a technique called ionic gelation. In this technique, electrostatic interaction occurs between the positively charged chitosan and negatively charged sodium tripolyphosphate (TPP), giving rise to robust nanoparticles that encapsulate the vaccine antigen [9]. This technique is recommended because it does not require extra factors like high temperatures and toxic solvents, creates nanoparticles having appropriate size(100-500nm) and facilitates the regulated release of antigens by varying the chitosan formulation and cross-linking parameters [10].

Chitosan-Based Nanovaccines Against Newcastle Disease:

During the past fifteen years, different scientists have effectively manufactured chitosan-based nanovaccines against ND. Different nanovaccines include the Recombinant protein vaccines, live attenuated vaccines, and DNA vaccines. The recombinant protein subunit vaccines are delivered to the body using chitosan nanoparticles as carriers. The second method is to position a weakened Newcastle disease virus inside the chitosan nanoparticles, and the third method includes a DNA that contains instructions for producing the viral antigen instead of carrying the virus or protein [11]. The first efficient method developed by researchers using the gelation technique was to trap the La Sota strain of NDV inside a chitosan nanoparticle. This formulation is favoured because it allows the slow release of the viral antigen instead of releasing all at once, protects the vaccine virus from environmental degradation, and preserves its biological activity as compared to a non-coated vaccine. Chitosan-based NDV nanoparticles stimulated enhanced mucosal (IgA) and systemic (IgG) immune responses in chickens. They also boosted the T cell production in the spleen and delivered better protection against a highly virulent Newcastle disease virus than traditional vaccines [12].

Scientists utilizing quaternized chitosan derivatives (O-2′-chloride chitosan and N-2-hydroxypropyl trimethylammonium chloride chitosan) as NDV DNA vaccine carriers which exibit promising results. Strong cellular and mucosal immune responses were the outcome of these compounds' increased solubility and positive charge, which also improved transfection efficiency and antigen expression in the respiratory mucosa. In contrast to

control birds immunized with conventional vaccinations, which showed 20% mortality and severe tissue damage, vaccinated birds challenged with virulent NDV demonstrated 100% protection with no clinical symptoms or microscopic lesions [13].

Advantages of Chitosan Nanovaccines in Poultry Production:

When compared to traditional ND vaccines, chitosan nanovaccines have better immunogenic qualities. Higher titers of particular antibodies (IgG and especially IgA), improved T-lymphocyte proliferation responses, increased production of interleukin-4 (IL-4) and interferon-gamma (IFN-γ), and better protection rates after virulent NDV challenge have all been reported in numerous field trials and experimental studies [14]. Chitosan nanovaccines administered intranasally or orally efficiently activate mucosal immunity at the respiratory and gastrointestinal mucosae, in contrast to traditional vaccines that mainly produce systemic immunity. A vital first line of defense is provided by the production of mucosal IgA antibodies, which stop viruses from attaching to and entering natural infection sites. This benefit is especially crucial for preventing airborne illnesses like Newcastle disease, where mucosal immunity is crucial [15]. Intranasal, oral, intramuscular injection, and even aerosol spray are some of the ways that chitosan nanovaccines can be delivered, giving vaccination programs flexibility to accommodate different production methods and management techniques. Because they eliminate the need for individual bird confinement and injection, intranasal or oral immunization techniques are very beneficial in terms of labor needs and poultry stress. Chitosan nanovaccines make mass vaccination techniques using spray or drinking water delivery systems possible, increasing immunization coverage in large commercial operations [16].

Chitosan nanovaccines have considerable long-term economic benefits due to their reduced cold-chain requirements, longer shelf life, fewer vaccine doses required, and easier administration routes, even though their initial research and development expenditures may be high. The capacity to retain vaccinations without constant refrigeration removes a significant financial burden for chicken farmers in developing nations with limited resources. Additionally, better defense against ND lowers mortality, treatment expenses, and output losses linked to the disease, giving farmers significant financial gains [17].

Future Perspectives and Challenges:

Creating genotype-matched chitosan nanovaccines that target the NDV strains common in endemic areas is an important line of inquiry. Reverse genetics and synthetic virology techniques can produce live attenuated viruses from currently circulating genotype VII and other common genotypes, which can then be encapsulated in chitosan nanoparticles, as an alternative to continuing to rely on vaccine strains that are decades old [18]. Subsequent studies emphasizes manfacturing of chimeric vaccines containing antigens from multiple genotypes of NDV, as well as multivalent nanovaccines, is able to protect against ND and other important poultry diseases, including infectious bronchitis, infectious laryngotracheitis, and avian influenza. Due to its multifunctional characteristics, chitosan can enclose numerous antigens or transport multiple vaccine constituents simultaneously, making it a favourable delivery vehicle for single-dose vaccinations that offer wide-ranging immunity against various pathogens [19].

Real-world efficacy of chitosan-based nanovaccines should be demonstrated via large-scale field studies executed within various chicken production systems, geographic areas, and environmental conditions. Investigations determine the ideal immunization schedule, analyze the period, protective immune responses in different poultry breeds, and verify vaccine effectiveness in combating numerous NDV genotypes. Effective field validation demands joint efforts from research teams, poultry farmers, and veterinary extension services [20].

Conclusion:

Current ND vaccine formulations commonly offer inadequate cross-immunity against genetically variable NDV strains, leading to continued serious concern for the worldwide poultry sector. Nanoparticle-based vaccine delivery platforms, especially using chitosan, provide a favourable strategy owing to biodegradation capability, tissue compatibility, and ability to improve antigenicity, mucosal immune response, environmental resilience, and simple administration. Research revealed that a chitosan-based vaccine increased immune protection and decreased the infection and death rate in domestic birds. Moreever their better storage life and decrease the requirement for a cold chain system, making them beneficial for developing regions. However, effective market introduction demands coordination among scientists, vaccine developers, regulatory agencies, and commercial poultry producers. Future studies emphasize the formation of a polyvalent nanovaccine, finalizing regulatory evaluations, large-scale production, and confirming vaccine efficacy via comprehensive field investigations. Chitosan-based nanovaccines have the potential to greatly improve Newcastle disease management, increase the sustainability of poultry production, and improve the lives of millions of people who depend on poultry farming worldwide with sustained investment and concerted international effort.

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